Sports Medicine
https://doi.org/10.1007/s40279-021-01624-5

SYSTEMATIC REVIEW

Effect of Interval Training on the Factors Influencing Maximal Oxygen Consumption: A Systematic Review and Meta-Analysis

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Accepted: 7 December 2021

Abstract

Background The maximal rate of oxygen consumption (VO_{2max}) is an important measure in exercise science as it is an indicator of cardiorespiratory fitness. Individual studies have identified central and peripheral adaptions to interval training that may underlie improvements in VO_{2max}, but there is no compilation of results.

Objective We aimed to systematically review the adaptive responses to high-intensity interval training (HIIT) and sprint interval training (SIT) on the central and peripheral factors influencing VO_{2max} in healthy individuals.

Data Sources SPORTDiscus and MEDLINE (up to and including 13 June, 2020) were explored to conduct the literature search.

Study Selection Reviewed studies met the following criteria: (1) were in the English language; (2) prospective in nature; (3) included at least three interval sessions or were at least 1 week in duration; (4) contained HIIT or SIT; (5) involved participants between the ages of 18 and 65 years; and (6) included at least one of the following central (blood volume, plasma volume, hemoglobin mass, left ventricular mass, maximal stroke volume, maximal cardiac output) or peripheral factors (capillary density, maximal citrate synthase activity, mitochondrial respiration associated with VO_{2max}).

Results Thirty-two studies (369 participants, 49 were female) were included in the quantitative analyses, consisting of both HIIT ($n=18$) and SIT ($n=17$) interventions. There were only statistically significant changes in hematological measures (plasma volume) following HIIT. There was a significant increase in left ventricular mass following HIIT (7.4%, $p<0.001$) and SIT (5.3%, $p=0.007$) in inactive individuals, though the change following SIT may be misleading. There was only a significant increase in maximal stroke volume (14.1%, $p=0.015$) and maximal cardiac output (12.6%, $p=0.002$) following HIIT. In addition to central factors, there was a significant increase in capillary density (13.8%, $p<0.001$) following SIT in active individuals. With respect to maximal citrate synthase activity, there were improvements following HIIT (20.8%, $p<0.001$) and SIT (15.7%, $p<0.001$, $I^2=97\%$) in active individuals. The results for mitochondrial respiration suggested that there was no statistically significant improvement following HIIT (5.0%, $p=0.585$).

Conclusions Improvements in the central and peripheral factors influencing VO_{2max} were dependent on the interval type. Only HIIT led to a statistically significant improvement in cardiac function. Both HIIT and SIT increased maximal citrate synthase activity, while changes in other peripheral measures (capillary density, mitochondrial respiration) only occurred with SIT.

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Published online: 18 January 2022

Key Points

High-intensity interval training can produce improvements in central factors influencing maximal oxygen consumption including plasma volume, left ventricular mass, maximal stroke volume, and maximal cardiac output.

Sprint interval training may be the optimal method of interval training to improve peripheral factors influencing maximal oxygen consumption such as skeletal muscle capillary density, maximal citrate synthase activity, and mitochondrial respiration.

The strength of the conclusions and implementation are limited by the small number of studies of interval training responses in trained individuals and by small sample sizes, a lack of control groups, and reporting biases.

1 Introduction

The maximal rate of oxygen that can be utilized by an individual (VO_{2max}) is an indicator of cardiorespiratory fitness and can impact endurance sport performance [1]. The maximal rate of oxygen consumption can be influenced by a number of factors including age [2] and physical activity level [3]. In addition, different forms of aerobic exercise such as continuous and interval training can lead to improvements in VO_{2max} [4]. When compared with continuous training, interval training has been shown to produce a 1–2% greater improvement in VO_{2max}, and can do so with considerably less training volume [4].

Interval training can be further divided into high-intensity interval training (HIIT) and sprint interval training (SIT). High-intensity interval training consists of repeated bouts of exercise at a power or velocity within the severe intensity domain [5]. Common measures used to define the lower border of the severe domain include critical power, maximal lactate steady state, and the second ventilatory threshold. The highest power or velocity that can still allow for the attainment of a VO_{2max} demarcates the upper border of the severe intensity domain. Sprint interval training is performed at power outputs or velocities above those associated with VO_{2max} in the extreme intensity domain [6]. Both forms of interval training produce similar improvements in VO_{2max}, but have different effects on endurance performance [7]. This may imply that there are mechanistic differences between the two forms of interval exercise.

A comprehensive review by Bassett and Howley [1] provides a list of key variables for physiologists to consider when studying the mechanisms associated with improvements in performance related to VO_{2max}. Central factors can include pulmonary diffusing capacity, respiratory function, maximal cardiac output (CO_{max}), and the oxygen carrying capacity of the blood. The peripheral factors primarily include determinants of the ability of the working muscle to uptake oxygen from the capillaries and its subsequent utilization by the mitochondria. While both factors can influence oxygen consumption, there has been an ongoing debate whether VO_{2max} is limited by central or peripheral factors.

Central adaptations, specifically, increases in CO_{max}, are strongly correlated with increases in VO_{2max} [8]. Adaptive changes in CO_{max} are primarily a result of increases in maximal stroke volume (SV_{max}) [9]. Therefore, the structure and function of the left ventricle itself should be considered when discussing potential limiting factors for VO_{2max}. A cross-sectional study of elite athletes found that endurance athletes have a significantly larger left ventricle chamber size when compared with athletes in non-aerobically focused sports [10]. The training-induced increase in chamber size and left ventricular mass (LVM) can lead to a greater SV_{max} [11] and CO_{max}, leading to an increase in VO_{2max} [8]. Increases in blood volume (BV), plasma volume (PV), red blood cell expansion, and hemoglobin mass (HbM) are also important central factors influencing VO_{2max} [12]. An increase in red blood cell volume can lead to an enhanced oxygen-carrying capacity of the blood [13]. A greater PV (hypervolemia) produces an increase in venous return with subsequent increases in SV_{max}, CO_{max}, and oxygen delivery [14, 15].

Maximal intensity exercise performed at sea level has not been shown to influence pulmonary diffusing capacity in healthy individuals [16]. Previous literature has demonstrated that trained individuals experience a greater degree of oxygen desaturation during exercise than untrained individuals [17]. However, there are several factors that can limit oxygen saturation during exercise including those related to oxygen delivery, such as CO_{max}, and the oxygen-carrying capacity of the blood. As the literature suggests that the pulmonary system may not influence VO_{2max} in healthy individuals, it will not be addressed in this review.

The ability to transport oxygen within skeletal muscle is a peripheral adaptation essential for aerobic metabolism. A dense capillary network promotes the diffusion of oxygen from the arterial system to the exercising muscles [1]. There is a strong correlation between capillary density (CD) and VO_{2max}, indicating that the degree of muscle capillarization can influence oxygen uptake [18, 19]. Endurance athletes have been shown to have a greater degree of capillarization than untrained individuals [20]. Increases in CD have been shown to occur in as little as 8 weeks following a continuous

training program in untrained individuals [21], suggesting that changes in CD are an adaptive response to exercise training.

Training-induced mitochondrial biogenesis represents another important peripheral adaption. Mitochondrial biogenesis has been defined as the incorporation of new proteins into pre-existing sub-compartments and protein complexes [22]. However, there is no consensus on how to accurately measure mitochondrial biogenesis. Changes in mitochondrial content, mitochondrial protein synthesis (mitoPS), and mitochondrial respiratory function have all been reported as an indication of training-induced mitochondrial adaptations [23]. Both mitochondrial content and mitochondrial respiratory function have been correlated with VO_{2max} [24]. Maximal citrate synthase (CS_{max}) activity and mitochondrial protein abundance are commonly used as biomarkers of mitochondrial content, whereas measurements of mitochondrial respiration (mitoR) are used to assess mitochondrial respiratory function [23]. Given that training-induced changes in these parameters, as well as mitoPS, are not necessarily linked, it is essential to assess as many of these parameters as possible.

A recent meta-analysis attempted to address the central vs peripheral limitation debate. Montero et al. conducted a meta-regression that included both inactive and active individuals (aged 22–28 years). This analysis showed that there is a strong correlation between increases in CO_{max} and increases in VO_{2max} (effect size = 0.91; 95% confidence interval [CI] 0.25–1.56, $p = 0.006$), and that there is no correlation between changes in arterio-venous oxygen difference and VO_{2max} (effect size = 0.20; 95% CI − 0.27 to 0.67, $p = 0.4$) [8]. This indicates that central factors may be more important to improve VO_{2max}. The review included a wide range of continuous and interval training studies [8]. The results of the review did not show a significant effect of training load or duration on maximal CO_{max} but did observe an increased effect on arteriovenous difference in studies with greater load or duration [8].

Although it has been shown that both forms of interval training improve VO_{2max} [25, 26], there is no consensus on which training method is optimal. Despite the fact that individual studies have identified central and peripheral adaptions to interval training that may underlie improvements in VO_{2max}, a compilation of the results of these studies is lacking. In addition, it would be noteworthy to differentiate between HIIT and SIT when examining the results, as there is evidence that they lead to differences in performance adaptations [7]. This is important because these training interventions may induce different physiological adaptations that are responsible for the performance gains. The objective of this article was to systematically review the effect of interval training on the central and peripheral factors that influence VO_{2max} in healthy individuals.

2 Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was used as the protocol for the design of the review [27]. The PRISMA guidelines include a 27-item checklist considered to improve reporting transparency, thereby limiting the risk of publication and selection bias [27].

2.1 Eligibility Criteria

2.1.1 Inclusion Criteria

Studies were selected for the review if they met the following criteria: (1) were in English; (2) were prospective in nature; (3) completed at least three interval sessions and were at least 1 week in duration [28, 29]; (4) included a HIIT or SIT group; (5) included participants between the ages of 18 and 65 years; and (6) included outcomes that would assess changes in central (BV, PV, HbM, LVM, SV_{max}, CO_{max}) or peripheral factors (CD, CS_{max} activity, mitoR) associated with VO_{2max}.

2.1.2 Exclusion Criteria

Studies were excluded if participants were postmenopausal, overweight, had pathology, or if the training program or outcome was inappropriate for this analysis for the following reasons: (1) training program not clearly defined; (2) included HIIT and SIT in the same program; (3) included additional exercise that was not quantified; (4) contained nutritional interventions (supplements, hydration, fed state); (5) were subject to changes in environmental conditions (heat/cold, altitude, hypoxia/hyperoxia); (6) identified the inclusion of recovery types (cryotherapy, compression garments); and (7) included pharmacological agents.

2.2 Information Sources

An electronic search was performed on 13 June, 2020 and included all publication years up to and including the date the search was conducted. The two databases, SPORTDiscus (EBSCOHost) and MEDLINE (OVID), were used to conduct the systematic literature search.

2.3 Search Strategy

2.3.1 Search String

The search string utilized in the meta-analysis by Rosenblat et al. was used to conduct the search as it provided an inclusive set of a results [7]. Key search terms that were produced from reviewing previous literature and using several synonyms of the different forms of interval training were grouped and searched within the article title and abstract, and keywords using the search conjunction 'OR'. The search string used was as follows: "(interval training OR interval exercise OR anaerobic interval* OR aerobic interval* OR high intensity interval* OR sprint interval* OR intermittent exercise OR intermittent training OR repeated sprint)".

2.3.2 Search Limits

The following limits were selected: (1) English language; (2) humans; and (3) journal article.

2.4 Study Records

2.4.1 Data Management

The search results were downloaded and imported into Reference Manager EndNote X9. Reference Manager was used to remove duplicates and to screen titles and abstracts, and full-text articles. A data collection spreadsheet in Microsoft Excel 365 was created using the Cochrane Data Extraction and Assessment Form template. All data extracted were entered into the spreadsheet.

2.4.2 Selection Process

The titles, abstracts, and full-text articles were independently screened by the lead author (MR). A second author (CG) was consulted if there was uncertainty about article eligibility. Disagreements were resolved through a discussion between the authors, with a third (ST) to be consulted if the first two authors could not reach agreement. The rationale for excluding articles was documented.

2.4.3 Data Collection Process

One author (either MR or ST) was responsible for collecting the data and the second author (MR or ST) checked the extracted data. Disagreements were discussed between the two authors with a third to be consulted if the first two authors could not reach agreement.

2.5 Data Items

The following data were extracted from each of the articles that were included in the review: study methodology (study design and duration); the participant characteristics (sex, age, height, mass, training status, baseline VO_{2max}); intervention description (interval type, exercise mode, training program duration, interval sessions performed each week, interval work-bout duration, interval work-bout intensity [expressed as a percentage of the power (W_{peak}) or velocity associated with VO_{2max}/VO_{2peak} or percentage of maximal heart rate, interval repetitions]); and outcome measures including VO_{2max}, BV, PV, HbM, LVM, CO_{max}, SV_{max}, CD, CS_{max} activity, and mitoR. Training volume was calculated as the product of training program duration (weeks) * interval work-bout duration * interval work-bout intensity * interval repetitions.

Training status was categorized into inactive (not engaged in deliberate physical activity), active (participate in a non-structured exercise program), and trained (structured training program that is specific to a mode of exercise). High-intensity interval training exercise was classified as repeated bouts of exercise that occur at a power output or velocity between the second ventilatory threshold and VO_{2max}. Sprint interval training included exercise performed at a power output or velocity above those associated with VO_{2max}. Measurements of maximal mass-specific mitochondrial function ($CI+II_p$) were used to quantify mitoR.

Data conversions were performed to determine values for missing data as well as to standardize scores to allow for a consistent interpretation of the results using the same methods described in the study by Rosenblat et al. [30]. In brief, the correction factor, $\text{Factor} = 1.8596 \times \text{TestDuration}^{-0.242}$, was used to standardize exercise intensity obtained from incremental exercise testing protocols that exceeded 12 min in duration. The standard deviation (SD) was estimated by using t values derived from the p value in instances where the standard error of the mean or SD were not available using the following formula: $\text{SD} = \sqrt{n}\left(\frac{\bar{x}_1 - \bar{x}_2}{t}\right)$, where $\bar{x}_1$ is the mean baseline value and $\bar{x}_2$ is the mean value at the end of the interval training program. A p value expressed using an inequality (e.g., '<') was considered as an equality (e.g. '='), providing a more conservative estimate of the SD. Delta scores were converted to a percentage change using the following formula: $\%\text{Delta} = \left(\frac{\text{Delta}}{\bar{x}_1} \times 100\right)$, where Delta is the difference between $\bar{x}_2$ and $\bar{x}_1$.

2.6 Risk of Bias of Individual Studies

The PEDro scale is a 10-point ordinal scale used to determine the internal validity of a study. The specific methodological components assessed include: (1) randomization; (2) concealed allocation; (3) baseline comparison; (4) blind participants; (5) blind therapists; (6) blind assessors; (7) adequate follow-up; (8) intention-to-treat analysis, (9) between-group comparisons; and (10) point estimates and variability [31]. Participant eligibility is also a component of the PEDro scale; however, it is not included in the final 10-point score.

2.7 Data Synthesis

Separate meta-analyses were conducted for studies that were sufficiently homogeneous. Specifically, pooled analyses were performed for studies that included individuals of similar training status (inactive, active, or trained) and for studies that incorporated interventions of similar interval type (HIIT or SIT). The %Delta scores were pooled using the metafor package (version 2.4-0) in R (version 4.0.2) using a random-effects model and the DerSimonian-Laird estimator.

2.8 Assessment of Heterogeneity and Risk of Bias Across Studies

The I^2 statistic was used to describe the degree of statistical heterogeneity by determining the percentage of the total variation in the estimated effect across studies. I^2 values of 25%, 50%, and 75% were considered as low, moderate, and high degrees of statistical heterogeneity [32]. The relationship between the effect size and the sample size was determined visually using a funnel plot. Egger's test was used to quantitatively assess for a small sample size bias [33].

3 Results

The dataset used in the quantitative analysis are available in Appendix S1 of the Electronic Supplementary Material (ESM). All figures and tables in this review include the data for studies that were in the quantitative analysis. Additional figures not provided in the results can be found in Appendix S2 of the ESM.

3.1 Study Selection

The databases SPORTDiscus and MEDLINE were used to perform the search, which yielded a total of 9453 results. Following the removal of 3032 duplicates, 6421 titles and abstracts were screened. A total of 58 full-text articles were screened for eligibility. Thirty-three studies with a total of 38 separate groups were included in the qualitative analysis and 32 studies with a total of 37 groups were included in the quantitative analysis (Fig. 1). Two pairs of publications, Burgomaster et al. [34] and Howarth et al. [35], as well as Christensen et al. [36] and Jacobs et al. [24], used data from the same datasets.

3.2 Study Characteristics

The studies included in the quantitative analyses had a total of 369 participants (age = 24.0 ± 2.9 years, 49 were female) who were classified as inactive ($n = 109$), active ($n = 215$), or trained ($n = 45$) individuals. There were 35 separate interval training groups, of which 18 were HIIT and 17 were SIT. Exercise mode included cycling and running. The HIIT programs consisted of intervals that ranged from 30 s to 5 min in work-bout duration at an exercise intensity range from 73 to 100% of W_{peak}. The SIT program intervals ranged from 2 to 60 s in work-bout duration at an exercise intensity range from 117% of W_{peak} to all-out effort. See Tables 1 and 2 for full details.

3.3 Risk of Bias Within Studies

The PEDro scores for the individual studies can be found in Table 3. There were no studies that included concealed allocation, subject blinding, or therapist blinding. All studies included measures of point estimates and variability. However, only 1 of the 33 studies reported all group means and SDs for baseline, follow-up, or change scores for the outcomes included in this review [55].

3.4 Results of Individual Studies

The outcomes for the individual studies on the effect of HIIT and SIT on the central and peripheral factors influencing VO_{2max} are presented in Tables 4 and 5.

3.5 Synthesis of Results

3.5.1 Effect of Interval Training on Changes in VO_{2max}

The influences of HIIT and SIT on changes in VO_{2max} are presented in Figs. 2 and 3. There was no significant difference in improvement between HIIT and SIT. Training status had a significant impact on change in VO_{2max} following HIIT, with trained individuals improving by 5.7% (95% CI 4.1–7.4, $p < 0.001$), active individuals by 9.7% (95% CI 7.0–12.3, $p < 0.001$), and inactive individuals by 21.4% (95% CI 18.1–24.7, $p < 0.001$). There was a similar pattern of improvement in VO_{2max} following SIT with trained individuals improving by 3.7% (95% CI 1.1–6.2, $p = 0.005$), active individuals by 7.2% (95% CI 5.6–8.9, $p < 0.001$), and inactive individuals by 14.1% (95% CI 9.8–18.3, $p < 0.001$).

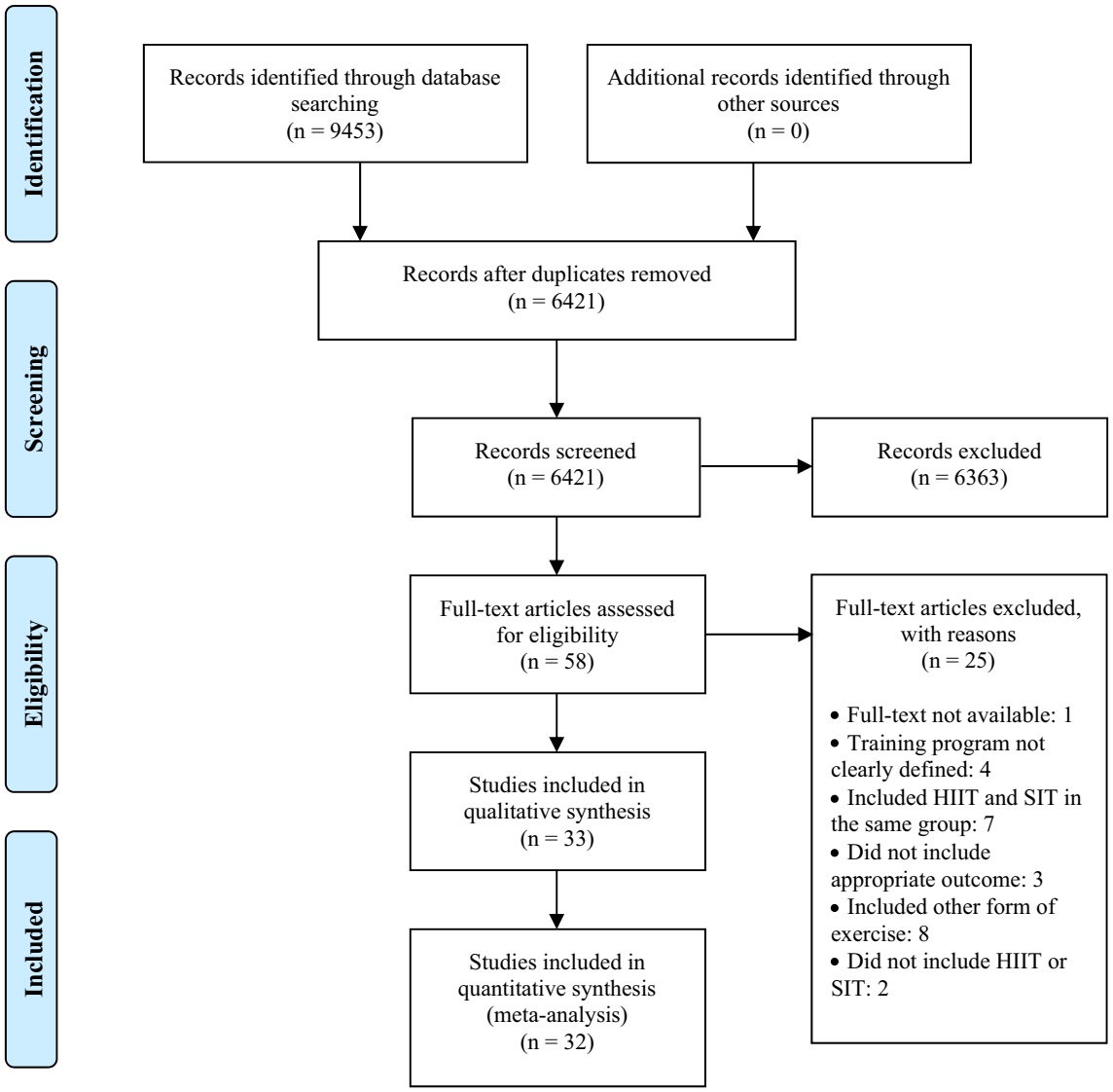

Fig. 1 PRISMA flow diagram. *HIIT* high-intensity interval training, *SIT* sprint interval training

To account for potential sex-based differences, a subgroup analysis was also performed to compare groups that consisted of male individuals ($n = 22$), female individuals ($n = 2$), and those that combined male and female individuals ($n = 5$). There was no significant difference in the change in VO_{2max} between studies that included male vs female individuals or for male individuals vs groups that combined male and female individuals following HIIT or SIT.

3.5.2 Effects of Interval Training on Central Factors Influencing VO_{2max}

The results from the studies included in the qualitative analysis are presented in Table 4 and the results from studies included in the quantitative analysis are presented in Figs. 4 and 5. There was a significant improvement in PV following HIIT in active individuals (8.2%, 95% CI 3.0–13.4). There was one outlier, which when removed increased the change in PV to 10.9% (95% CI 8.1–13.6, $p < 0.001$). There were no other statistically significant changes in hematological measures (BV, PV, HbM) following HIIT or SIT. Regarding cardiac morphology, there was a significant increase in LVM following HIIT of 7.4% (95% CI 4.8–10.1, $p < 0.001$) and SIT of 5.3% (95% CI 1.4–9.1, $p = 0.007$) in inactive individuals. In addition, there was a significant increase in SV_{max} (14.1%, 95% CI 2.7–25.4, $p < 0.02$) and CO_{max} (12.6%, 95% CI 4.8–20.4, $p < 0.002$) following HIIT.

Table 1 Study characteristics

Study	Study design	Participant characteristics								Intervention			Outcomes
		Group	*n*	Age (years)		Sex	Training status	VO_{2max} ($mL \cdot kg^{-1} \cdot min^{-1}$)		Weeks	Interval type	Exercise mode	
				Mean	SD			Mean	SD				
Bonafiglia et al. [37]	NCT	1	14	22.0	2.5	M	Active	42.4	7.7	6	SIT	Cycling	CD
Burgomaster et al. [38]	CT	1	8	22.0	2.8	B	Active	44.6	9.0	2	SIT	Cycling	CS_{max}
Burgomaster et al. [39]	CT	1	8	21.0	2.8	M	Active	48.7	7.2	2	SIT	Cycling	CS_{max}
Burgomaster et al. [34], Howarth et al. [35]	CT	1	10	24.0	3.2	B	Active	41.0	6.3	6	SIT	Cycling	CS_{max}
Christensen et al. [36], Jacobs et al. [24]	NCT	1	16	27.0	3.0	M	Active	43.0	6.0	2	HIIT	Cycling	CS_{max}, PV, HbM, mitoR
Dawson et al. [40]	NCT	1	9	22.0	2.0	M	Active	57.0	7.2	6	SIT	Running	CS_{max}
Esfandiari et al. [41]	RCT	1	8	24.5	3.1	M	Active	39.5	7.1	2	HIIT	Cycling	PV
Gillen et al. [42]	CT	1	9	27.0	7.0	M	Inactive	32.0	7.0	12	SIT	Cycling	CS_{max}
Gorostiaga et al. [43]	CT	1	6	27.0	1.3	B	Active	36.3	2.7	8	HIIT	Cycling	CS_{max}
Granata et al. [44]	RCT	1	11	20.5	1.4	M	Active	45.1	7.2	4	HIIT	Cycling	CS_{max}, mitoR
Granata et al. [44]	RCT	2	9	21.3	2.6	M	Active	47.1	3.8	4	SIT	Cycling	CS_{max}, mitoR
Gurd et al. [45]	NCT	1	9	23.4	3.3	B	Active	45.0	5.4	6	HIIT	Cycling	CS_{max}
Helgerud et al. [46]	RCT	1	10	24.6	3.8	M	Active	57.9	6.8	8	HIIT	Running	CO_{max}, SV_{max}
Hoier et al. [47]	NCT	1	9	31.7	n/a	M	Inactive	37.9	n/a	4	SIT	Cycling	CD
Huang et al. [48]	RCT	1	18	21.4	1.7	M	Inactive	34.7	5.1	6	HIIT	Cycling	LVM
Jalaludeen et al. [49]	RCT	1	21	21.0	1.7	B	Inactive	n/a	n/a	4	SIT	Cycling	LVM
Kohn et al. [50]	NCT	1	18	n/a	n/a	M	Trained	67.0	5.0	6	HIIT	Running	CD, CS_{max}
Laursen et al. [51]	CT	1	8	26.5	6.9	M	Trained	65.6	6.5	4	HIIT	Cycling	PV
Laursen et al. [51]	CT	2	9	24.6	7.0	M	Trained	66.4	4.5	4	HIIT	Cycling	PV
Laursen et al. [51]	CT	3	10	25.0	5.8	M	Trained	63.7	3.8	4	SIT	Cycling	PV
Little et al. [52]	NCT	1	7	21.0	1.0	M	Active	46.0	2.0	2	HIIT	Cycling	CS_{max}
MacDougall et al. [53]	NCT	1	12	22.7	2.0	M	Active	50.8	1.8	7	SIT	Cycling	CS_{max}
Macpherson et al. [54]	CT	1	10	24.3	3.3	F	Active	46.8	5.1	6	SIT	Running	CO_{max}, SV_{max}
Matsuo et al. [55]	RCT	1	12	29.8	6.9	M	Inactive	39.8	7.9	8	HIIT	Cycling	LVM
Matsuo et al. [56]	RCT	1	14	27.2	6.4	M	Inactive	41.9	5.6	8	HIIT	Cycling	PV, LVM
Matsuo et al. [56]	RCT	2	14	26.4	6.5	M	Inactive	43.9	6.7	8	SIT	Cycling	PV, LVM
Parra et al. [57]	RCT	1	5	23.6	2.4	M	Active	n/a	n/a	2	SIT	Cycling	CS_{max}
Parra et al. [57]	RCT	2	5	23.6	2.4	M	Active	n/a	n/a	6	SIT	Cycling	CS_{max}
Perry et al. [28]	NCT	1	9	23.0	2.1	M	Active	n/a	n/a	2	HIIT	Cycling	CS_{max}
Raleigh et al. [58]	NCT	1	23	20.4	1.8	M	Active	48.7	6.4	4	SIT	Cycling	CO_{max}, CD, CS_{max}
Scribbans et al. [59]	CT	1	6	20.7	3.8	M	Active	51.9	5.1	6	SIT	Cycling	CD
Slørdahl et al. [60]	NCT	1	12	21.9	1.3	F	Inactive	42.6	2.9	8	HIIT	Running	LVM
Talanian et al. [61]	NCT	1	8	22.0	2.8	F	Active	36.3	10.4	2	HIIT	Cycling	CS_{max}

Table 1 (continued)

Study	Study design	Participant characteristics							Intervention			Outcomes
		Group	*n*	Age (years)		Sex	Training status	VO_{2max} ($mL \cdot kg^{-1} \cdot min^{-1}$)	Weeks	Interval type	Exercise mode	
				Mean	SD			Mean SD				
Warburton et al. [29]	RCT	1	6	29.0	4.0	M	Active	38.7 7.9	12	HIIT	Cycling	PV, CO_{max},LVM, SV_{max}
Weston et al. [62]	NCT	1	6	22.5	3.0	M	Trained	66.2 2.6	4	HIIT	Cycling	CS_{max}
Wright et al. [63]	RCT	1	7	25.5	5.0	M	Active	n/a n/a	2	HIIT	Cycling	PV

B both, *CD* capillary density, CO_{max} maximal cardiac output, CS_{max} maximal citrate synthase activity, *CT* controlled trial, *F* female, *HbM* hemoglobin mass, *HIIT* high-intensity interval training, *LVM* left ventricular mass, *M* male, *mitoR* mitochondrial respiration, *n/a* data not available, *NCT* non-controlled trial, *PV* plasma volume, *RCT* randomized controlled trial, *SD* standard deviation, *SIT* sprint interval training, SV_{max} maximal stroke volume, VO_{2max} maximal rate of oxygen consumption

3.5.3 Effects of Interval Training on Peripheral Factors Influencing VO_{2max}

The results from the studies included in the qualitative analysis are presented in Table 5 and those included in the quantitative analysis are presented in Figs. 6 and 7. There was a statistically significant increase in CD following SIT of 13.8% (95% CI 6.5–21.2, $p < 0.001$) in active individuals. With respect to CS_{max} activity, there was a similar improvement ($p = 0.869$) following HIIT (20.8%, 95% CI 15.7–25.8, $p < 0.001$) and SIT (15.7%, 95% CI 6.3–25.0, $p = 0.001$) in active individuals. There was one outlier in the pooled data for SIT [40], which when removed increased the changes in CS_{max} activity to 20.9% (95% CI 12.0–29.7, $p < 0.001$). The results for mitoR suggest that there was no statistically significant improvement following HIIT (5.0%, 95% CI − 13.0 to 23.0, $p = 0.585$).

3.6 Assessment of Heterogeneity and Risk of Bias Across Studies

The studies consisted of several different designs including non-controlled [pre-post] ($n = 14$), controlled ($n = 9$), and randomized ($n = 10$) studies. A subgroup analysis on the influence of study design on the pooled effect of change in VO_{2max} showed that there was no difference between the non-controlled and controlled studies.

There was a high degree of statistical heterogeneity in the pooled results for changes in VO_{2max} following HIIT ($I^2 = 84\%$). When grouped by training status, there was a decrease in I^2 values for inactive ($I^2 = 0\%$), active ($I^2 = 46\%$), and trained ($I^2 = 0\%$) individuals. There was a moderate degree of statistical heterogeneity following SIT (57%), which also decreased when grouped by training status with values of 0%, 22%, and 0% for inactive, active, and trained individuals, respectively. When groups were separated by sex, there was no change in statistical heterogeneity for HIIT or SIT.

There was also evidence of moderate-to-high degrees of statistical heterogeneity in the pooled results for the central and peripheral factors influencing VO_{2max}. Specifically, in the results for changes in BV ($I^2 = 90\%$), PV ($I^2 = 75\%$), and mitoR ($I^2 = 79\%$) following HIIT in active individuals, and for changes in CS_{max} activity ($I^2 = 97\%$) following SIT in active individuals. There was one outlier [24] in the pooled analysis of PV following HIIT and another outlier [40] in the pooled analysis for CS_{max} activity following SIT. The degree of statistical heterogeneity only changed upon removal of the study in the PV analysis ($I^2 = 0\%$).

A visual inspection of a funnel plot for changes in VO_{2max} following HIIT and SIT indicated the presence of asymmetry. The results from Egger's test suggested the presence of

Table 2 Interval training program description

Study	Group	Interval type	Exercise mode	Sessions per week	Interval repetitions	Work-bout intensity ($\%W_{peak}/\%V_{peak}$)	Work-bout duration (min)	Recovery-bout mode	Recovery-bout duration (min)	Training duration (weeks)	Total sessions
Bonafiglia et al. [37]	1	SIT	Cycling	4	8	170	0.33	Passive	0.17	6	24
Burgomaster et al. [38]	1	SIT	Cycling	3	6	Maximal effort	0.50	Passive	4.00	2	6
Burgomaster et al. [39]	1	SIT	Cycling	3	6	Maximal effort	0.50	Passive	4.00	2	6
Burgomaster et al. [34], Howarth et al. [35]	1	SIT	Cycling	3	6	Maximal effort	0.50	Passive	4.50	6	18
Christensen et al. [36], Jacobs et al. [24]	1	HIIT	Cycling	3	10	100	1.00	Active	1.25	2	6
Dawson et al. [40]	1	SIT	Running	3	30	90	0.06	Passive	0.33	6	18
Esfandiari et al. [41]	1	HIIT	Cycling	3	10	98	1.00	Active	1.25	2	6
Gillen et al. [42]	1	SIT	Cycling	3	3	Maximal effort	0.33	Active	2.00	12	36
Gorostiaga et al. [43]	1	HIIT	Cycling	3	20	100	0.50	Passive	0.50	8	24
Granata et al. [44]	1	HIIT	Cycling	3	6	88	4.00	Active	2.00	4	12
Granata et al. [44]	2	SIT	Cycling	3	7	Maximal effort	0.50	Passive	4.00	4	12
Gurd et al. [45]	1	HIIT	Cycling	3	10	90	4.00	Passive	2.00	6	18
Helgerud et al. [46]	1	HIIT	Running	3	4	n/a	4.00	Active	3.00	8	24
Hoier et al. [47]	1	SIT	Cycling	3	24	117	1.00	Passive	1.50	4	12
Huang et al. [48]	1	HIIT	Cycling	5	5	80	3.00	Active	3.00	6	30
Jalaludeen et al. [49]	1	SIT	Cycling	3	3	Maximal effort	0.50	Active	2.00	4	12
Kohn et al. [50]	1	HIIT	Running	2	6	100	2.50	Passive	1.50	6	12
Laursen et al. [51]	1	HIIT	Cycling	2	8	100	2.40	Passive	4.80	4	8
Laursen et al. [51]	2	HIIT	Cycling	2	8	100	2.60	Passive	4.00	4	8
Laursen et al. [51]	3	SIT	Cycling	2	12	175	0.50	Passive	4.50	4	8
Little et al. [52]	1	HIIT	Cycling	3	10	100	1.00	Active	1.25	2	6
MacDougall et al. [53]	1	SIT	Cycling	3	7	Maximal effort	0.50	Active	3.00	7	21
Macpherson et al. [54]	1	SIT	Running	3	5	Maximal effort	0.50	Active	4.00	6	18
Matsuo et al. [55]	1	HIIT	Cycling	3	3	83	3.00	Active	2.00	8	24
Matsuo et al. [56]	1	HIIT	Cycling	5	3	85	3.00	Active	2.00	8	40
Matsuo et al. [56]	2	SIT	Cycling	5	7	120	0.50	Passive	0.25	8	40
Parra et al. [57]	1	SIT	Cycling	7	5	Maximal effort	0.38	Passive	0.75	2	14
Parra et al. [57]	2	SIT	Cycling	3	5	Maximal effort	0.38	Passive	0.75	6	15
Perry et al. [28]	1	HIIT	Cycling	4	10	90	4.00	Passive	2.00	2	7
Raleigh et al. [58]	1	SIT	Cycling	4	8	170	0.33	Passive	0.17	4	16
Scribbans et al. [59]	1	SIT	Cycling	4	8	170	0.33	Passive	0.17	6	24
Slørdahl et al. [60]	1	HIIT	Running	3	8	n/a	2.50	Active	2.50	8	24
Talanian et al. [61]	1	HIIT	Cycling	4	10	90	4.00	Passive	2.00	2	7

Table 2 (continued)

Study	Group	Interval type	Exercise mode	Sessions per week	Interval repetitions	Work-bout intensity ($\%W_{peak}/\%V_{peak}$)	Work-bout duration (min)	Recovery-bout mode	Recovery-bout duration (min)	Training duration (weeks)	Total sessions
Warburton et al. [29]	1	HIIT	Cycling	3	8	90	2.00	Active	2.00	12	36
Weston et al. [62]	1	HIIT	Cycling	2	7	80	5.00	Active	1.00	4	6
Wright et al. [63]	1	HIIT	Cycling	3	10	98	1.00	Active	1.25	2	6

HIIT high-intensity intervaltraining, *min* minutes, *n/a* data not available, *SIT* sprint interval training, V_{max} maximal velocity, V_{peak} peak velocity, W_{peak} peak power output

a small sample size bias for both HIIT ($p < 0.004$) and SIT ($p < 0.007$).

4 Discussion

4.1 Summary of Evidence

4.1.1 Effect of Interval Training on Changes in VO_{2max}

The results of the pooled analysis indicated that there was no statistically significant difference in the change in VO_{2max} following HIIT and SIT. This finding is in agreement with a previous meta-analysis that included studies with direct comparisons of HIIT to SIT [7]. However, in the current review, there was a moderate-to-large degree of statistical heterogeneity in the pooled results for HIIT ($I^2 = 84\%$) and SIT ($I^2 = 57\%$). To account for the statistical heterogeneity, sub-group analyses were performed for sex and training status.

Sex did not influence the change in VO_{2max} or the degree of statistical heterogeneity following HIIT or SIT. There was a significant difference in the change in VO_{2max} when participants were grouped by training status, which subsequently led to a decrease in the statistical heterogeneity of the results. This classification method was also shown to be valid for examining changes in time-trial performance following HIIT and SIT [30]. As participant training status was shown to strongly influence the response to interval training on changes in VO_{2max} (and time-trial performance [30]), it was appropriate to group the results for the central and peripheral physiological measures using the same classification.

4.1.2 Effects of Interval Training on Central Factors Influencing VO_{2max}

Hematological changes take place prior to changes in cardiac morphology as PV expansion can occur following a single session of exercise [12]. Changes in PV, and subsequent changes in BV, directly influence cardiac function by altering venous return, SV_{max}, and CO_{max} [11]. There is a decrease in PV immediately post-high-intensity interval exercise (HIIE) [64] and sprint interval exercise (SIE) [65], likely as a result of both sweating and a shift in intravascular fluids [66]. In any event, there is an increase in hematocrit immediately following HIIE [64] and SIE [65]. However, hematocrit has been shown to return to normal levels within 3 h post-SIE [67] and 24-h post-HIIE [64, 68]. This is associated with an increase in plasma albumin levels following interval exercise, which remain elevated for at least 24 h [68]. Albumin is responsible for at least 75% of the oncotic pressure of plasma [68], therefore, it acts as the driving force to pull

Table 3 Risk of bias of individual studies

Study	Eligibility	Random allocation	Concealed allocation	Baseline comparison	Blind subjects	Blind therapists	Blind assessors	Adequate follow-up	Intention to treat	Between-group comparison	Point estimates/variability
Bonafiglia et al. [37]	0	0	0	0	0	0	0	1	0	0	1
Burgomaster et al. [38]	1	1	0	1	0	0	0	1	1	1	1
Burgomaster et al. [39]	1	0	0	0	0	0	0	1	0	1	1
Burgomaster et al. [34], Howarth et al. [35]	1	0	0	1	0	0	0	1	1	1	1
Christensen et al. [36], Jacobs et al. [24]	1	0	0	0	0	0	0	1	1	0	1
Dawson et al. [40]	0	0	0	0	0	0	0	1	0	0	1
Esfandiari et al. [41]	1	1	0	1	0	0	0	1	1	1	1
Gillen et al. [42]	1	1	0	1	0	0	0	1	0	1	1
Gorostiaga et al. [43]	0	0	0	1	0	0	0	0	0	1	1
Granata et al. [44]	0	1	0	1	0	0	0	1	0	1	1
Gurd et al. [45]	1	0	0	0	0	0	0	1	0	1	1
Helgerud et al. [46]	1	1	0	0	0	0	0	0	0	1	1
Hoier et al. [47]	0	0	0	0	0	0	0	1	0	1	1
Huang et al. [48]	1	1	0	1	0	0	0	1	1	1	1
Jalaludeen et al. [49]	1	1	0	1	0	0	0	1	0	1	1
Kohn et al. [50]	1	0	0	0	0	0	0	1	1	0	1
Laursen et al. [51]	0	0	0	1	0	0	0	1	0	1	1
Little et al. [52]	0	0	0	1	0	0	0	1	1	1	1
MacDougall et al. [53]	0	0	0	1	0	0	0	0	0	1	1
Macpherson et al. [54]	1	1	0	0	0	0	0	1	1	1	1
Matsuo et al. [55]	1	1	0	1	0	0	0	1	1	1	1
Matsuo et al. [56]	1	1	0	1	0	0	1	1	1	1	1
Parra et al. [57]	0	1	0	1	0	0	0	1	1	1	1
Perry et al. [28]	0	0	0	1	0	0	0	1	0	1	1
Raleigh et al. [58]	1	0	0	1	0	0	0	1	0	1	1
Scribbans et al. [59]	0	0	0	0	0	0	0	0	0	1	1
Slørdahl et al. [60]	0	0	0	0	0	0	0	1	1	0	1
Talanian et al. [61]	0	0	0	0	0	0	0	1	1	1	1
Warburton et al. [29]	0	1	0	0	0	0	0	0	0	1	1
Weston et al. [62]	0	0	0	0	0	0	0	1	0	0	1
Wright et al. [63]	1	1	0	0	0	0	0	1	1	1	1

A score of 0 indicates that the component was absent or not reported and a score of 1 indicates that the component was present

Table 4 Effects of interval training on central factors influencing maximal oxygen consumption at various activity levels

Outcome	Interval type	Training status	Study	Group	Units	Pre		Post		Delta		*P* value
						Mean	SD	Mean	SD	Mean	SD	
PV	HIIT	Inactive	Matsuo et al. [56]	1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.93
		Active	Esfandiari et al. [41]	1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	< 0.001
			Jacobs et al. [24]	1	mL	3286.0	141.0	3284.0	108.0	− 2.0	369.2*	0.983
			Warburton et al. [29]	1	$mL \cdot kg^{-1}$	37.0	7.0	41.0	5.0	4.0	3.8*	< 0.05
			Wright et al. [63]	1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	< 0.005
		Trained	Laursen et al. [51]	1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
			Laursen et al. [51]	2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
	SIT	Inactive	Matsuo et al. [56]	2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.15
		Trained	Laursen et al. [51]	3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
HbM	HIIT	Active	Jacobs et al. [24]	1	g	854.0	30.0	850.0	29.0	− 4.0	60.8*	0.796
BV	HIIT	Inactive	Matsuo et al. [56]	1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.94
		Active	Helgerud et al. [46]	1	mL	5810.0	840.0	5950.0	800.0	140.0	n/a	n/a
			Jacobs et al. [24]	1	mL	5786.0	233.0	5765.0	199.0	− 21.0	485.7*	0.865
			Warburton et al. [29]	1	$mL \cdot kg^{-1}$	61.0	11.0	67.0	9.0	6.0	3.7	< 0.05
	SIT	Inactive	Matsuo et al. [56]	2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.32
LVM	HIIT	Inactive	Huang et al. [48]	1	g	153.4	3.6	169.1	3.9	15.7	31.4*	< 0.05
			Matsuo et al. [55]	1	g	101.0	17.0	106.0	15.0	5.1	8.4	0.06
			Matsuo et al. [56]	1	g	102.0	15.0	109.1	n/a	7.3	7.1	< 0.01
			Slørdahl et al. [60]	1	g	123.9	22.7	139.2	23.8	15.3	16.0*	0.007
		Active	Esfandiari et al. [41]	1	g	182.4	49.1	191.2	58.2	8.8	36.4	0.52
	SIT	Inactive	Jalaludeen et al. [49]	1	g	129.0	36.0	132.0	36.0	3.0	22.6*	0.55
			Matsuo et al. [56]	2	g	103.0	14.0	111.8	n/a	6.5	8.8	< 0.02
CO_{max}	HIIT	Active	Helgerud et al. [46]	1	$L \cdot min^{-1}$	28.5	3.1	31.4	2.5	3.0	2.8*	< 0.01
			Warburton et al. [29]	1	$L \cdot min^{-1} \cdot m^{-2}$	10.0	3.0	12.0	4.0	2.0	1.9*	< 0.05
	SIT	Active	Macpherson et al. [54]	1	$L \cdot min^{-1}$	24.5	1.2	24.4	1.2	− 0.1	n/a	n/a
			Raleigh et al. [58]	1	$L \cdot min^{-1}$	19.9	3.3	20.9	3.9	1.0	n/a	n/a
SV_{max}	HIIT	Active	Helgerud et al. [46]	1	$mL \cdot beat^{-1}$	144.2	21.9	159.2	21.9	15.0	14.3*	< 0.01
			Warburton et al. [29]	1	$mL \cdot beat^{-1} \cdot m^{-2}$	56.0	16.0	69.0	23.0	13.0	12.3*	< 0.05
	SIT	Active	Macpherson et al. [54]	1	$mL \cdot beat^{-1}$	138.0	7.0	135.0	7.0	− 3.0	n/a	n/a

BV blood volume, CO_{max} maximal cardiac output, *HbM* hemoglobin mass, *HIIT* high-intensity interval training, *LVM* left ventricular mass, *n/a* data not available, SV_{max} maximal stroke volume, *PV* plasma volume, *SD* standard deviation, *SIT* sprint interval training, *SD estimated from *p*-value

Table 5 Effects of interval training on peripheral factorsinfluencing maximal oxygen consumption at various activity levels

Outcome	Interval type	Training status	Study	Group	Units	Pre		Post		Delta		*P* value
						Mean	SD	Mean	SD	Mean	SD	
CD	HIIT	Trained	Kohn et al. [50]	1	cap·fibre^{-1}	5.6	1.2	6.0	0.9	0.3	1.3	0.39
	SIT	Inactive	Bonafiglia et al. [37]	1	cap·mm^{-2}	375.1	70.8	433.6	86.2	51.9	60.9	< 0.05
			Hoier et al. [47]	1	cap·mm^{-2}	n/a	n/a	n/a	n/a	n/a	n/a	n/a
		Active	Raleigh et al. [58]	1	cap·mm^{-2}	468.0	87.0	533.0	70.0	65.0	149.6*	< 0.05
			Scribbans et al. [59]	1	cap·mm^{-2}	n/a	n/a	n/a	n/a	n/a	n/a	< 0.05
CS_{max} activity	HIIT	Inactive	Gorostiaga et al. [43]	1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
		Active	Christensen et al. [36]	1	µmol·min^{-1}·mg protein^{-1}	120.0	35.0	128.0	19.0	8.0	53.9*	0.65
			Granata et al. [44]	1	mol·h^{-1}·kg protein^{-1}	8.0	2.2	8.6	1.8	0.6	2.3	0.244
			Gurd et al. [45]	1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	< 0.05
			Little et al. [52]	1	mmol·kg protein^{-1}·h^{-1}	2.9	0.4	3.5	0.9	0.6	0.6	0.01
			Perry et al. [28]	1	mmol·min^{-1}·kg ww^{-1}	23.1	3.7	28.5	4.6	5.3	1.5	< 0.001
			Talanian et al. [61]	1	mmol·min^{-1}·kg wm^{-1}	24.5	5.4	29.3	4.6	4.9	6.0	< 0.05
		Trained	Kohn et al. [50]	1	µmol·min^{-1}·g dw^{-1}	32.0	8.7	30.8	10.4	−1.2	7.5	0.49
			Weston et al. [62]	1	µmol·g protein^{-1}·min^{-1}	n/a	n/a	n/a	n/a	n/a	n/a	n/a
	SIT	Inactive	Gillen et al. [42]	1	mmol·kg protein^{-1}·h^{-1}	3.0	0.8	4.5	0.9	1.5	1.1	< 0.05
		Active	Burgomaster et al. [38]	1	mol·kg protein^{-1}·h^{-1} (wet wt)	4.0	2.0	5.5	0.9	1.5	1.6	< 0.05
			Burgomaster et al. [39]	1	mol·kg protein^{-1}·h^{-1} (wet wt)	7.0	1.2	7.8	1.1	0.7	0.9	0.04
			Burgomaster et al. [34]	1	mol·kg protein^{-1}·h^{-1} (wet wt)	3.7	1.1	4.6	0.8	0.9	1.2	< 0.05
			Dawson et al. [40]	1	µmol·g^{-1} wet mass ·min^{-1}	10.0	1.4	6.8	0.9	−3.2	2.8*	0.01
			Granata et al. [44]	2	mol·h^{-1}·kg protein^{-1}	9.4	1.8	9.6	1.9	0.2	1.0	0.555
			MacDougall et al. [53]	1	mol·kg protein^{-1}·h^{-1}	n/a	n/a	n/a	n/a	n/a	n/a	< 0.05
			Parra et al. [57]	1	µmol·min^{-1}	28.1	2.4	38.0	1.6	10.7	0.6	< 0.05
			Parra et al. [57]	2	µmol·min^{-1}	33.1	3.6	42.5	2.8	9.4	0.7	< 0.05
			Raleigh et al. [58]	1	µmol·g protein^{-1}·min^{-1}	38.2	5.6	42.6	5.1	4.4	10.1*	< 0.05
MitoR (CI + CII_p)	HIIT	Active	Granata et al. [44]	1	pmol O_2·min^{-1}·mg wet wt^{-1}	68.1	11.6	65.6	7.7	−2.4	11.1	0.489
			Jacobs et al. [24]	1	pmol O_2·min^{-1}·mg wet wt^{-1}	86.9	4.1	99.8	6.0	12.9	24.1*	< 0.05
	SIT	Active	Granata et al. [44]	2	pmol O_2·min^{-1}·mg wet wt^{-1}	85.6	12.1	106.9	19.0	21.3	15.1	< 0.003

CD capillary density, CS_{max} maximal citrate synthase activity, *HIIT* high-intensity interval training, *mitoR* mitochondrial respiration, *n/a* data not available, *SD* standard deviation, *SIT* sprint interval training, *SD estimated from *p*-value

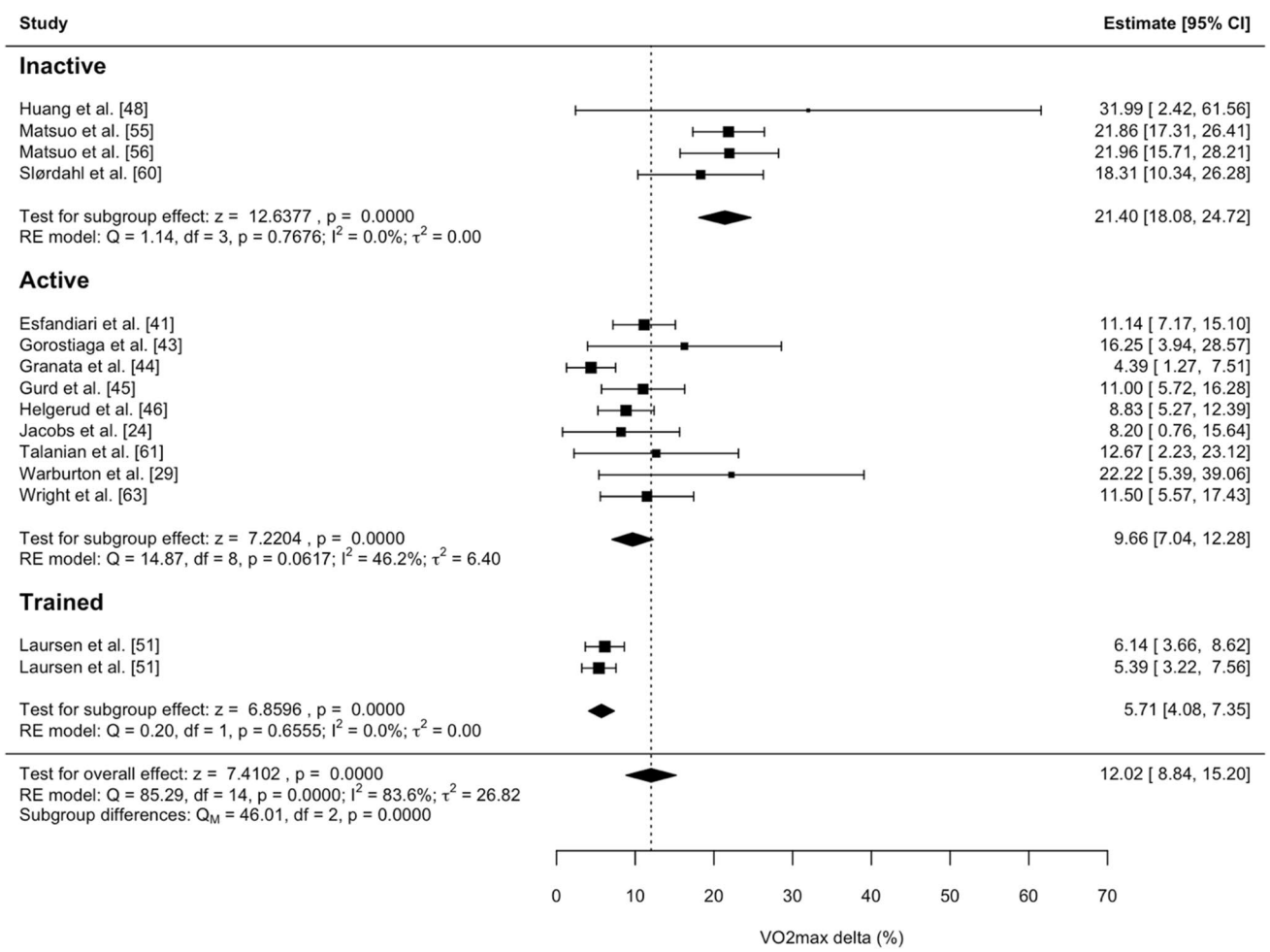

Fig. 2 Influence of training status on change in maximal oxygen consumption (VO_{2max}) following high-intensity interval training. *CI* confidence interval, *RE* random effects

fluid back into the vascular system and return hematocrit to pre-exercise levels.

The results of the meta-analysis suggest that there were no statistically significant changes in hematological measures following HIIT or SIT. There was a large degree of statistical heterogeneity in the pooled analyses for BV ($I^2 = 90\%$) and PV ($I^2 = 75\%$) in active individuals following HIIT. This was likely driven by the results of the study by Jacobs et al. [24], which did not show an improvement in BV or PV. Variations in the techniques used to determine the hematological measures may explain the differences in 2.7. Warburton et al. [29] and Wright et al. [63] determined BV and PV by using microhematocrit for estimations, whereas Jacobs et al. [24] used HbM determined from a carbon monoxide rebreather to estimate PV and BV. Only one study in the review assessed changes in HbM following interval training (HIIT), but there was no statistically significant change [24].

A seminal review by Montero et al. [12] explained that increases in PV will plateau in approximately 2 weeks following moderate-intensity continuous training (MICT). These findings are similar to the results of the current meta-analysis, which showed that HIIT produced improvements in PV in as early as 2 weeks, with no additional improvement following 12 weeks of training (beta = 0.3, 95% CI − 1.1 to 1.7, $p = 0.6519$, $I^2 = 83\%$) [Fig. 1 of the ESM]. Three of the studies in the analysis of PV included MICT as a comparator [29, 41, 63], which allowed for a pairwise meta-analysis of the two training types. The results showed there to be no difference in the change in the PV between HIIT and MICT (mean difference (MD) = 0.5%, 95% CI − 3.3 to 4.2, $p = 0.8106$, $I^2 = 0\%$) [Fig. 2 of the ESM].

Both HIIT and SIT were shown to produce increases in LVM (7.4% and 5.3%, respectively). These findings were lower than those in the study by Weiner et al. [69], which found improvements in LVM of 14% in 3 months and an additional 9% by 36 months. A meta-regression for training variable modifiers showed that both training duration (beta = − 1.5, 95% CI − 6.7 to 3.8, $p = 0.5834$, $I^2 = 26\%$) and

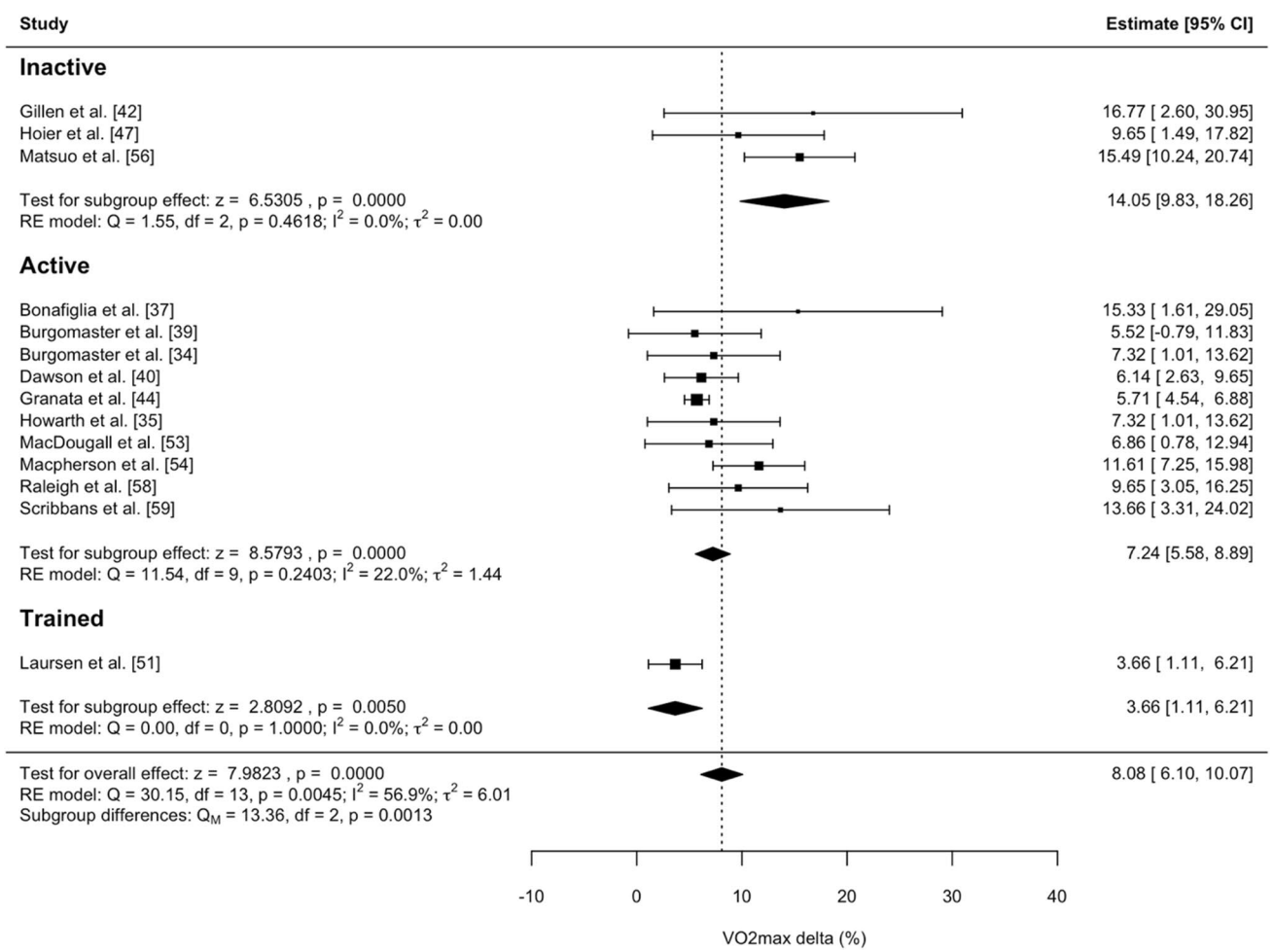

Fig. 3 Influence of training status on change in maximal oxygen consumption (VO_{2max}) following sprint interval training. *CI* confidence interval, *RE* random effects

training volume (beta = 0.0003, 95% CI − 0.0001 to 0.0006, $p = 0.1186$, $I^2 = 0\%$) did not influence the change in LVM following HIIT results (Fig. 3 of the ESM). However, the studies included in the analysis were only 6–8 weeks in duration. This may have been too brief a time-frame to observe a dose response relationship between training duration (weeks) with changes in LVM; as shown by Weiner et al. [69]. Three studies included a MICT comparison group [48, 55, 56], and therefore we conducted another pairwise meta-analysis comparing HIIT with MICT on LVM. The mean difference of the pooled results showed that HIIT produced a significantly greater improvement in LVM (MD = 4.5%, 95% CI 0.3–8.7, $p = 0.034$, $I^2 = 0\%$) (Fig. 4 of the ESM).

The pooled analysis for SIT on LVM may be questionable as only two studies were included in the analysis, with only the Matsuo et al. [56] study showing a significant improvement in LVM. This may be problematic because the training protocol used in the study by Matsuo et al. [56] vastly differed from that used in the other study [49]. In fact, the protocol closely resembled an intermittent form of HIIT that has been shown to be effective for improving VO_{2max} [70, 71]. The protocol in the Matsuo et al. [56] study included intermittent SIT consisting of 30-s work bouts that were of relatively low intensity (120% W_{peak}) followed by 15-s recovery bouts. The other SIT study, by Jalaludeen et al. [49], which did not show a significant improvement in LVM, incorporated a SIT protocol similar to those shown maximize time-trial performance [30], consisting of 30-s maximal effort sprints followed by relatively longer recovery bouts of 2 min.

There were quantitative data for two studies that included SV_{max} and CO_{max} with HIIT [29, 46], which showed improvements in both measures. The results of the study by Warburton et al. [29] showed a positive correlation between changes in SV_{max} ($r = 0.53$, $p < 0.05$) and CO_{max} ($r = 0.53$, $p < 0.05$) with changes in PV. Helgerud et al. [46] indicated that there was a relationship between the increases in SV_{max} and CO_{max} with increases in VO_{2max}. There were two SIT

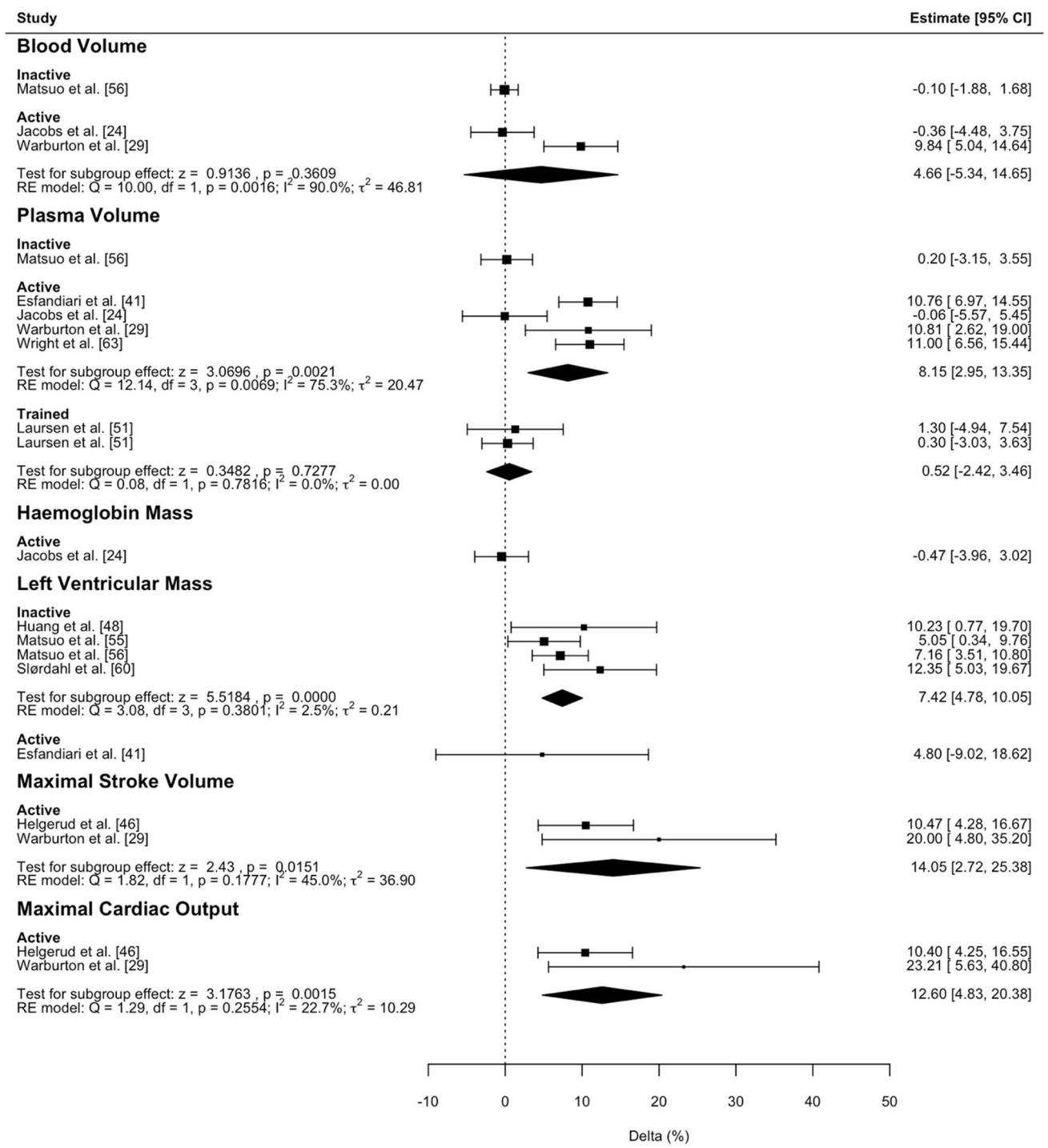

Fig. 4 Influence of high-intensity interval training on the central factors influencing maximal oxygen consumption. *CI* confidence interval, *RE* random effects

studies that included SV_{max} and CO_{max} but did not include effect sizes [54, 58]. Nevertheless, the authors stated that there were no improvements in either measure.

The study by Zafeirdis et al. may provide insight into how the exercise-induced responses to HIIE led to long-term adaptations in cardiac structure and function [72]. They investigated the acute effects of HIIE (2 min at 95% W_{peak} with a 2-min recovery) and SIE (30 s at 110% W_{peak} with a 30-s recovery) on central and peripheral hemodynamic responses in a group of active individuals. The results of

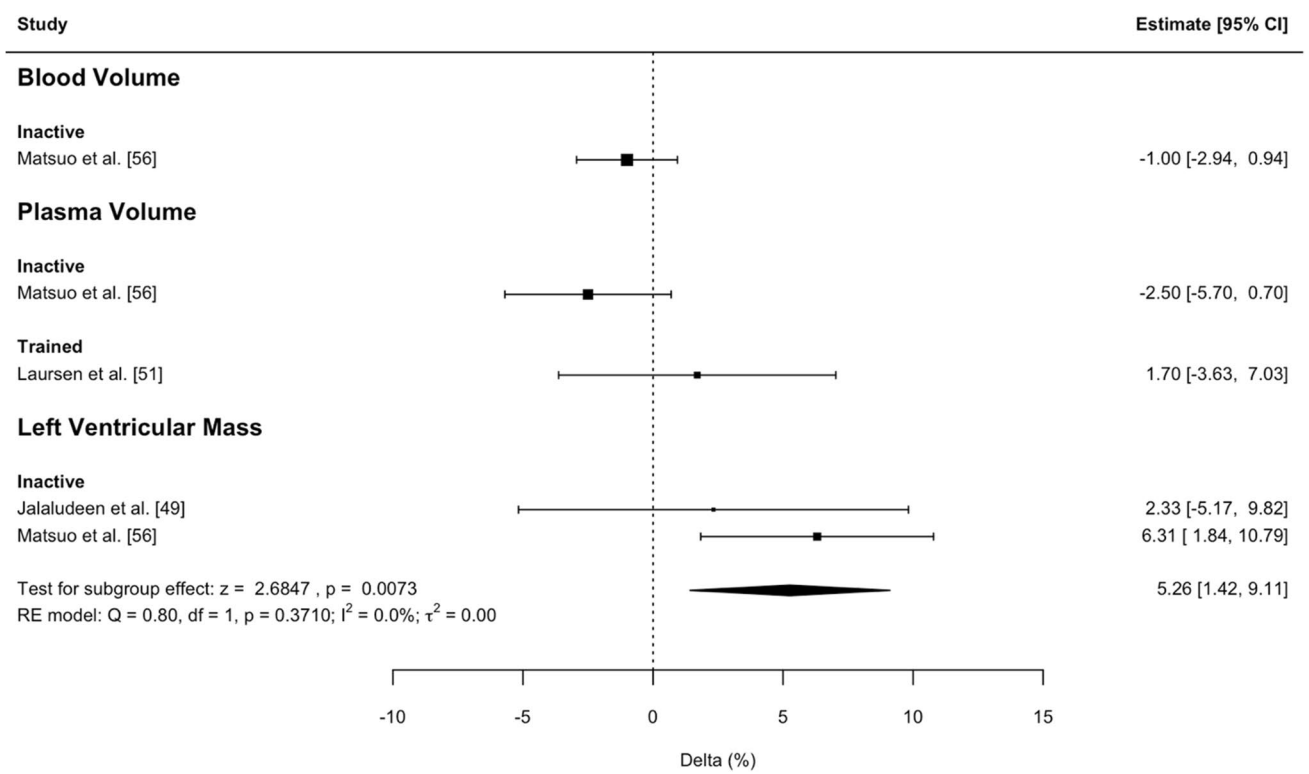

Fig. 5 Influence of sprint interval training on the central factors influencing maximal oxygen consumption. *CI* confidence interval, *RE* random effects

the study showed that CO increased during both HIIE and SIE. However, there was a 6% greater increase in peak CO and an 8% greater increase in average CO during HIIE [72]. The difference in CO was due to a 6% greater increase in average SV during HIIE when compared with SIE [72]. The higher SV_{max} may be associated with a greater stimulus for adaptation in cardiac morphology (i.e., changes in LVM). It is important to note that the intensity in the SIE group was well below that of a typical SIT program, which limits the ability to generalize the results.

4.1.3 Effects of Interval Training on Peripheral Factors Influencing $\dot{V}O_{2max}$

Improvement in performance is associated with an increased ability to transport oxygen into skeletal muscle through the capillary beds [18, 19]. The mechanical and metabolic stress produced during exercise can promote the growth of new capillaries [73]. Although exercise-induced changes in mRNA content are not necessarily correlated with training-induced changes in protein content [74], it is still informative to investigate these adaptations.

Vascular endothelial growth factor (VEGF) is considered to be the most pro-angiogenic factor in skeletal muscle [75]. Interval training has been shown to produce elevations in both the mRNA expression of VEGF as well as VEGF content [37, 47, 76–79]. There is evidence showing that SIE can lead to increased mRNA expression of VEGF in both inactive individuals [37, 47] and cyclists [77, 78]. High-intensity interval exercise can also promote mRNA expression of VEGF in cyclists and in swimmers [76]. A study by Casuso et al. directly compared the effects of both SIE and HIIE in a group of swimmers. The results of the study found that VEGF was only increased following HIIE [76]. Conversely, two studies [77, 78] employed a SIE protocol of similar duration and intensity to the Casuso et al. study [76] but reported an increase in VEGF [77]. A likely explanation for these discrepancies may relate to the different type of exercise (swimming [76] vs cycling [77, 78]) and muscle analyzed (triceps brachii [76] vs quadriceps femoris [77, 78]) in the above studies.

The one study that investigated the effects of HIIT on changes in CD did not show a statistically significant change post-training [50]. It is important to note that this study assessed changes in the number of capillaries per muscle fibre as opposed to the technique used in the other studies, which measured the cross-sectional area of capillaries. There were quantitative data available from two SIT studies that could be used to conduct a pooled analysis on changes in

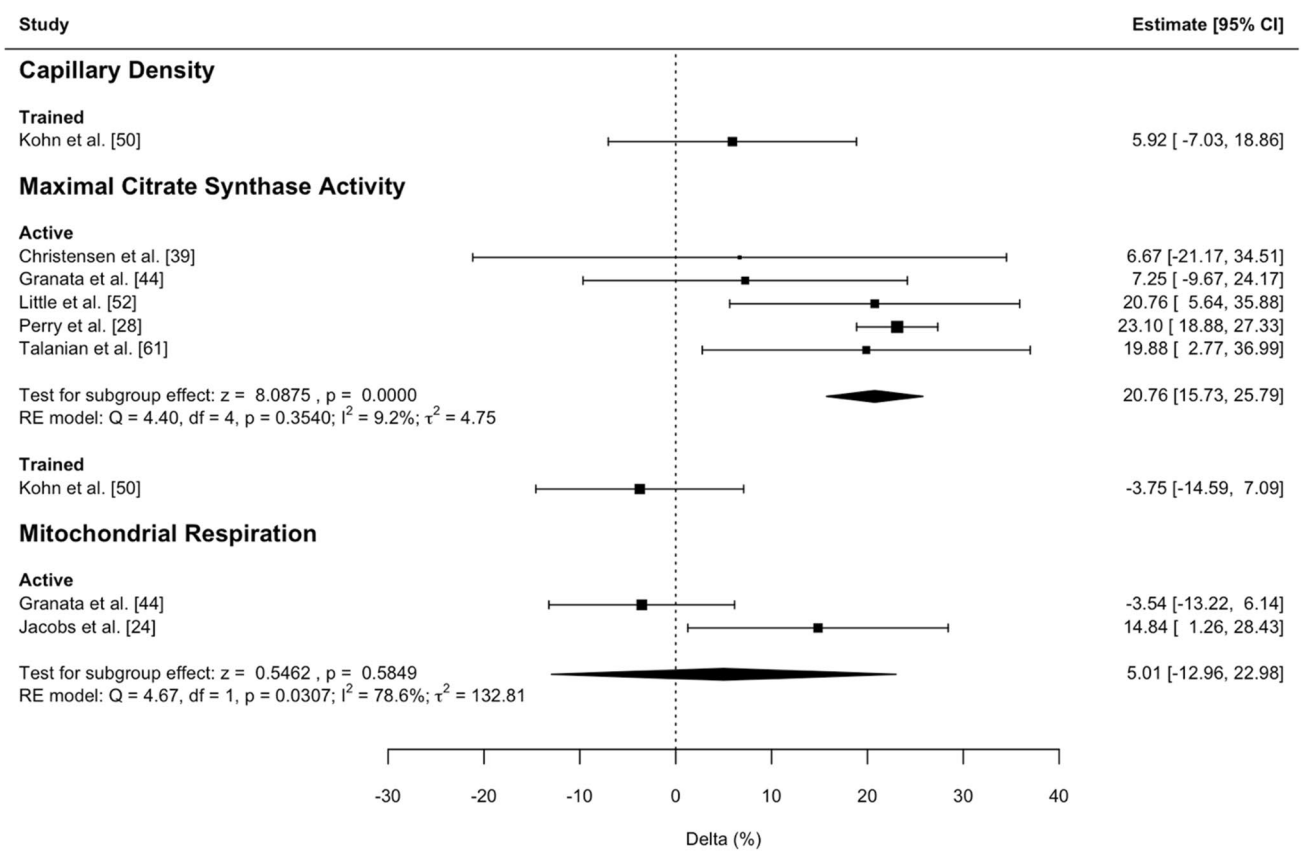

Fig. 6 Influence of high-intensity interval training on the peripheral factors influencing maximal oxygen consumption. *CI* confidence interval, *RE* random effects

CD [37, 58], with the results showing improvements. Separately, three out of four studies employing SIT reported an increase in CD [37, 80, 81], whereas one group observed no angiogenesis [47]. The three studies that indicated that angiogenesis occurred performed 20-s SIT bouts at 170% W_{peak} [37, 80, 81], which is at the high end of the SIT exercise intensity spectrum. The SIT study that did not show a statistically significant change in CD utilized 1-min bouts at 117% W_{peak} [47], which is at the low end of the SIT exercise intensity spectrum and close to exercise intensities usually employed during HIIT interventions. It is possible that greater exercise intensity induces the metabolic and physiological stress required to promote angiogenesis. However, previous investigations have demonstrated increases in CD following 9 weeks of moderate-intensity aerobic exercise [82]. Therefore, exercise intensity may not be the only contributing factor promoting angiogenesis.

In addition to improving the ability to deliver oxygen into skeletal muscle, it is important to consider the effect of interval training on commonly used markers of mitochondrial biogenesis and the subsequent changes in the ability of mitochondria to utilize oxygen for ATP production. Maximal citrate synthase activity is the most common biomarker of changes in mitochondrial content [83]. With respect to training-induced changes in CS_{max} activity, both HIIT and SIT interventions show similar results, with most studies demonstrating an increase. There was a large degree ($I^2 = 97\%$) of statistical heterogeneity in the pooled analysis for SIT. The study by Dawson et al. [40], which was the only study that showed a decrease in CS_{max} activity, incorporated work bouts that were approximately 5 s in duration; whereas the other studies included work bouts between 20 and 30 s [34, 38, 39, 44, 57, 58]. As previously discussed, there was no change in the statistical heterogeneity when the Dawson et al. [40] study was removed from the analysis. The variability of repeated muscle biopsies for measuring mitochondrial respiratory capacity has been shown to be as high as 15% [84], which may explain the limitations in interpreting the pooled analysis.

A previous analysis by Granata et al. [23] showed that training volume was moderately correlated ($r = 0.59$, $p < 0.001$) with changes in CS_{max} activity. Our analyses showed that training volume was not related to changes following HIIT (beta = 0.0003, 95% CI − 0.0004 to

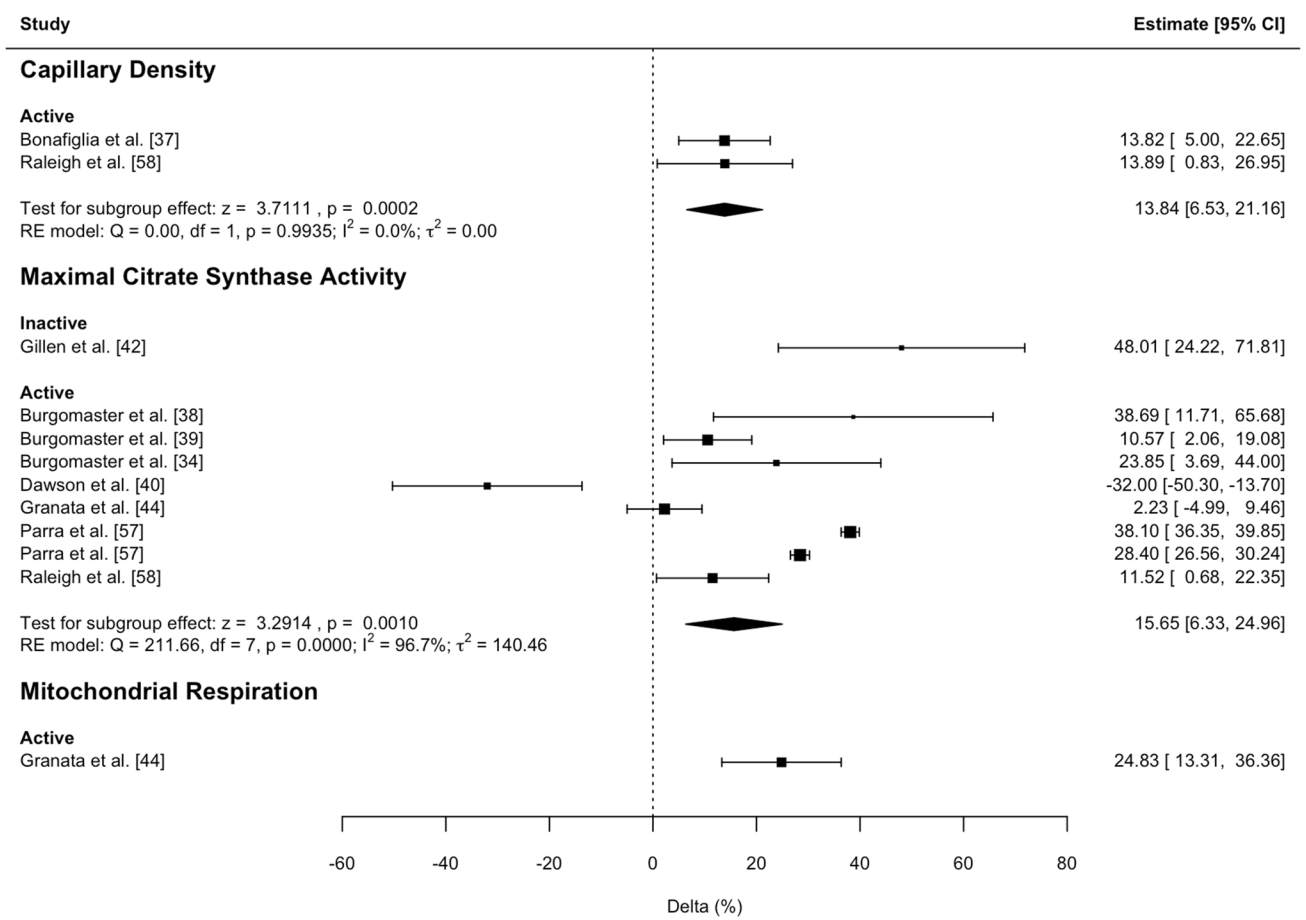

Fig. 7 Influence of sprint interval training on the peripheral factors influencing maximal oxygen consumption. *CI* confidence interval, *RE* random effects

0.0011, $p = 0.3813$, $I^2 = 10\%$) or SIT (beta = −0.002, 95% CI −0.006 to 0.0024, $p = 0.446$, $I^2 = 95\%$) [Fig. F5 of the ESM]. A likely reason explaining this discrepancy relates to the fact that the Granata et al. [23] study included HIIT, SIT, and MICT in the same analysis, whereas the analysis in the current review divided exercise types into different groups, and did not include studies assessing MICT.

There is evidence to suggest that there is a positive relationship between exercise intensity and increases in mitoR [23]. All the studies involving HIIT and SIT, except for the one HIIT group in the study by Granata et al. [44], reported a training-induced increase in mitoR [24, 44]. The reason for the lack of increase in mitoR in the HIIT group in the Granata et al. [44] study is likely due to the relatively lower intensity at which HIIT was performed; 73% of maximal power (W_{max}) when adjusted for testing protocol duration as suggested by Morton [85]. However, when changes in mitoR are normalized by unit of training time or training volume, SIT has been shown to be the superior form of exercise [23]. This is particularly important for elite athletes aiming to maximize their performance, and for normal populations for whom time availability often represents a limiting factor on their ability to train and maintain aerobic fitness.

4.2 Limitations

To the best of our knowledge, this review comprised all studies that investigated the effects of interval training on the central and peripheral factors associated with $\dot{V}O_{2max}$ in apparently healthy individuals. There are several limitations present at both the study and review level that may influence the interpretation of the results. Approximately half of the studies did not include a control group. This makes it difficult to determine if the observed improvements were by chance or due to the specifics of the intervention. Regarding the studies that included a comparison group, only half randomly allocated participants into their respective groups. The lack of randomization increases the potential for selection bias as well as the possibility that the results will be influenced by confounding variables.

Many of the studies included in this review had very small sample sizes with 20 of the 38 groups having fewer than ten participants, and all but two of the groups having fewer than 20 participants. Under-powered studies such as those included in this review, and many sport science studies [86], have a lower probability of determining the true effect [87]. In cases when a statistically significant effect is established, the magnitude of the effect may be exaggerated and also have a low positive predictive value [87].

There was a high degree of reporting bias as most of the studies (all but one) did not provide effect sizes and SDs for the baseline, follow-up, or change scores for at least one of the variables included in the review. The authors of the studies were contacted, but in instances when data were not successfully obtained, missing values for SDs were calculated by converting p values using t tests as described in Sect. 2.5. At its most conservative estimate ($p < 0.05$), SDs were approximately 25% greater than using the non-estimated values. Therefore, the pooled results of studies that included estimated SDs were likely to have larger CIs.

There are additional limitations with respect to the generalizability of the results of the current review. First, the review only included apparently healthy individuals. This was because there is evidence that the physiological response to exercise differs between healthy individuals and those who have pathology. This is most evident in individuals with cardiovascular disease [88, 89]. Another potential concern with including clinical populations, such as those with cardiovascular disease, is that many individuals with cardiovascular disease are taking medications that can blunt the exercise response, thereby limiting the stimulus required for adaptive changes [90, 91]. Second, because of the limited number of studies available for each variable, we were unable to determine the influence of programming characteristics on changes in outcomes. This would have been a beneficial analysis as performance outcomes (i.e., time-trial tests) following HIIT and SIT have been shown to be strongly influenced by different programming variables [30]. Finally, because the pooled analyses only consisted of within-group changes, as opposed to a comparison to control or another intervention, it would be difficult to determine if the change was due to other factors such as a performance bias [92].

4.3 Practical Application

The current review showed that there was no difference in the changes in VO_{2max} between HIIT and SIT, consistent with previous literature directly comparing HIIT with SIT [7]. However, there were differences in programming characteristics as the total training volume required for SIT was substantially less than that of HIIT. A recent meta-analysis by Rosenblat et al. investigated the influence of interval training programming variables on changes in time-trial performance and found that SIT only required a maximal training duration of 2 weeks [30]. Programs that were 4 weeks or longer were shown to be most advantageous when incorporating HIIT. The combination of these findings suggest that it may be most beneficial to incorporate a SIT program to produce a relatively quick improvement in VO_{2max} as well as in performance measures such as time-trial tests.

The results of this review suggest that improvements in VO_{2max} following HIIT and SIT may occur through both similar and different physiological mechanisms. Therefore, it may be beneficial to include both HIIT and SIT in a training program. With respect to changes in submaximal performance, Rosenblat et al. found that there is a 2% greater improvement in time-trial performance following HIIT compared to SIT [7]. Similarly, because of the greater training volume achievable, HIIT has been shown to promote larger increases in mitochondrial content, whereas the high exercise intensity associated with SIT programs has been shown to improve mitochondrial respiratory function [23]. Therefore, it would be optimal to include both forms of interval training in an intervention program as the differences in adaptive responses likely produce unique performance gains.

4.4 Future Directions

The objective of this article was to systematically review the effect of interval training on the central and peripheral factors that influence VO_{2max} in healthy individuals. The results of the meta-analysis showed that training status strongly influenced changes in VO_{2max}. However, there were limited studies ($n = 1$) conducted in trained individuals. Additional investigations in trained individuals are required to determine the impact of HIIT and SIT on the physiological factors that influence changes in VO_{2max}. In addition, this review only included apparently healthy individuals. Future reviews should consider the impact that interval training has on these physiological parameters in clinical populations to guide exercise prescription.

5 Conclusions

Improvements in central factors including cardiac function and blood volume are important to consider when attempting to maximize VO_{2max} adaptations. High-intensity interval training may produce greater increases in cardiac function (SV_{max} and CO_{max}) compared with SIT. Current literature indicates that neither HIIT nor SIT elicit increases in HbM. However, studies that are longer than 2–3 weeks in duration may be required before such adaptions can be determined. Sprint interval may have a greater influence on angiogenesis when compared with HIIT; however, there are limited

training studies that include HIIT interventions. Improvements in the specific measures associated with the central and peripheral factors influencing VO_{2max} are dependent on the interval type.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40279-021-01624-5.

Acknowledgements We thank the following authors for sharing data from their work to help with our analyses: Jacob Bonafiglia, Sam Esfandiari, Martin Gibala, Jenna Gillen, Jack Goodman, Tertius Kohn, Kathryn Myburgh, Jamie O'Driscoll, Christopher Perry, Lawrence Spriet, and Jason Talanian.

Declarations

Funding No sources of funding were used to assist in the preparation of this article.

Conflict of interest Michael Rosenblat, Cesare Granata, and Scott Thomas declare that they have no conflicts of interest relevant to the content of this review.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Availability of data and material All data supporting the results in this manuscript are available within the results sections, the cited articles, or the Electronic Supplementary Material. The R code used to conduct the analyses is available from the corresponding author upon reasonable request.

Authors' contributions Michael Rosenblat conceived and designed the study, performed the literature search, screening, study selection, data extraction, assessment of study quality and bias, statistical analyses and interpretation, and manuscript preparation. Cesare Granata participated in the statistical analyses and interpretation and manuscript preparation. Scott Thomas participated in study design, assessment of study quality and bias, and manuscript preparation.

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